

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT : **Franks et al.**
SERIAL NO. : **10/524,316**
FILED : **February 9, 2005**
FOR : **ANALGESIC AGENT FOR NEWBORN OR FETAL SUBJECTS**
EXAMINER : **E. Arnold**
GROUP ART UNIT : **1616**

COMMISSIONER FOR PATENTS
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DECLARATION UNDER 37 C.F.R. 1.132

SIR:

I, Dr. Aubrey Maze, declare as follows:

1. I am Chief Executive Officer of Valley Anesthesiology Consultants since 1982. This is a group of nearly 200 board certified anesthesiologists, who do the majority of the Pediatric anesthesia in Phoenix Arizona. I am also a Clinical Professor of Anesthesiology at the University of Arizona. I was the Assistant Professor in pediatric anesthesia at Stanford University from 1976 to 1979. I am board certified in anesthesia and pediatrics. Since 1998 I have been a senior examiner for the American Board of Anesthesiologists (ABA). I was Chief of Pediatric Anesthesia at Phoenix Children's Hospital 1984 to 1997. In 1990-1992 I was President of the Society for Pediatric Anesthesia.
2. I received my medical degree from University of Cape Town in 1970.
3. I have authored several articles relating to pediatric anesthesia and have lectured, at many National and International meeting relating the use of analgesic agents in the newborn and fetus. My primary interest is in clinical management of pediatric patients especially the neonate at time

of delivery or within the first 28 days of life when many procedures are required to enhance the quality of life of the neonate.

4. I have reviewed the above-identified application. I understand that the claims of the application are directed to methods of providing analgesia to newborn and fetal subjects in need of analgesia by administering to the newborn or the mother of the fetus, a therapeutically effective amount of xenon.

5. I have also reviewed the Office Action of October 15, 2007. I understand that the Examiner's position is that every fetus and newborn experiences pain as a result of the mechanical stresses the fetus is subjected to during the birthing process. As such, every fetus and newborn is in need of analgesia according to the Examiner.

6. While fetuses may experience pain during the birthing process, not every fetus or newborn that experiences pain is in need of analgesia. In fact, only a subset of the population of fetuses and newborns that will experience pain are need of analgesia. Such sub-population are those newborns or fetuses that will experience stress or pain sufficient to necessitate analgesia such as those that will undergo certain surgical procedures during or after delivery as well as those who will be treated for certain pathological conditions or exposed to certain non-surgical procedures.

7. Regarding surgical procedures, airway management procedures such as tracheostomy for management of cystic hygroma, lymphangioma of the intra-oral space, or haemangioma of the intra-oral space will expose the fetus or newborn to sufficient pain or stress to require administration of an analgesic agent during and/or prior to the procedure. Other relevant procedures are drainage of fluids in bodily cavities for conditions such as hydrocephalus and hydronephrosis. Certain *in utero* or emergent cardiac and abdomino-thoracic procedures also require administration of analgesic to the fetus or newborn such as a valvotomy for a hypoplastic heart or diaphragmatic surgery. In *in utero* abdominal wall procedures in newborns or fetuses suffering from gastroschisis or omphalocele may necessitate analgesia.

8. Regarding pathological conditions, newborns or fetuses who will be treated by exchange transfusion for hemolytic anemia due to rhesus incompatibility or ABO

incompatibility are also in need of analgesia.

9. Regarding non-surgical procedures that induce pain during delivery sufficient to necessitate administration of an analgesic agent, newborns that are delivered via assisted methods (i.e. forceps or ventouse) experience more stress than those that are not delivered via assisted methods (See attached article at Exhibit A: "Mode of delivery and subsequent stress response"). Therefore, in my opinion, newborns or fetuses who will require assisted delivery are in need of analgesia to alleviate such stress. Other procedures that necessitate administering an analgesic agent include instrumentation with forceps to treat pelvic cephalo-pelvic disproportion or manual correction to treat cephalo-pelvic disproportion such as dystocia. Another relevant non- surgical procedure is instrumentation such as ventouse extraction to treat a prolonged second stage of labor.

10. Therefore, not every fetus and newborn is in need of analgesia to alleviate the pain associated with childbirth (i.e. because of mechanical stresses experienced during childbirth). Specially, not every fetus or neonate will suffer sufficient pain prior, during or after childbirth such that they are in "need of analgesia" to warrant administration of a pharmaceutical agent such as xenon. Rather, as shown by the attached article and the categorization provided above, certain neonates or fetuses will experience more pain or stress than others and are therefore in need of an analgesic agent to relieve this pain or stress.

11. Even though all neonates may experience pain during the birthing process, I would not administer xenon to such patients on this basis alone. Rather other factors, as described above, would contribute to my decision to administer an analgesic to a fetus or newborn. Further, as with any pharmaceutical agent, I would not administer xenon to a newborn or to the mother of a fetus unless needed. Therefore, contrary to the Examiner's position, not all fetuses and newborns are "in need of analgesia" and the present claims are directed to administering xenon only to patients that are considered to be in such need.

12. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the patent or any reexamination certificate issued therefor.

Dated: 7.3.08


Dr. Aubrey Maze